SUPPORT FOR AMENDMENT

Claim 9 has been incorporated into Claim 1. Claims 17 and 18 have been amended to indicate their dependence on amended Claim 1. Claim 36 has been amended to indicate dependence on Claim 27. Claim 39 has been incorporated into Claim 38. Claims 9-16 and 39 have been cancelled. No new matter has been added.

Attached herewith is a marked-up version of the changes made to the claims by this amendment. The attached page is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE."

REQUEST FOR RECONSIDERATION

Drug release from polymeric implants is typically provided by a solution of a biodegradable polymer and a bioactive agent in a biocompatible solvent. The solution solidifies upon injection into the body to form a polymeric implant from which the agent is released. In some instances, this method yields zero-order release kinetics. However, zero-order release kinetics are not ideal for all therapies, and there is a need for biodegradable implants that can have a variety of drug release characteristics.

The present invention includes a composition for controlled release of a bioactive agent, comprising a biodegradable crystallizable polymer, a biodegradable amorphous polymer, a biocompatible solvent, and a bioactive agent. The present invention further includes a composition for controlled release of a bioactive agent, comprising a biodegradable crystallizable polymer and a biodegradable amorphous polymer. Crystallizable polymers, when crystallized, are semi-crystalline; and all semi-crystalline polymers are crystallizable.

In Table 1 in the Examples, a comparison is shown between a composition containing only a biodegradable amorphous polymer (PDLA, Example 5) and compositions which contain a biodegradable crystallizable polymer (PCL, Examples 1-4) alone or as a part of a combination with a biodegradable amorphous polymer. Figures 5 and 10, reproduced on the next page for convenience, illustrate the variation in release characteristics that can be provided by the presence of crystallizable polymer in the formulation.

Figure 5

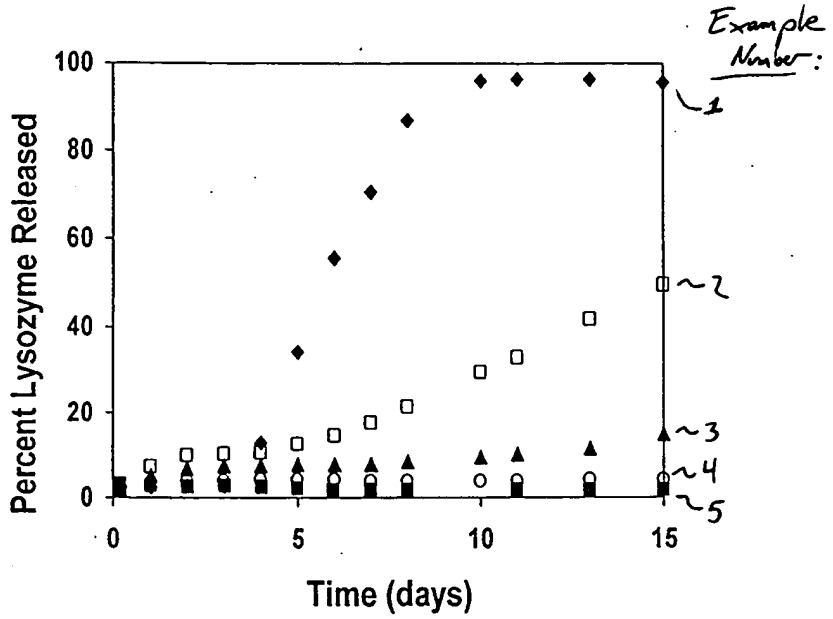

Figure 10

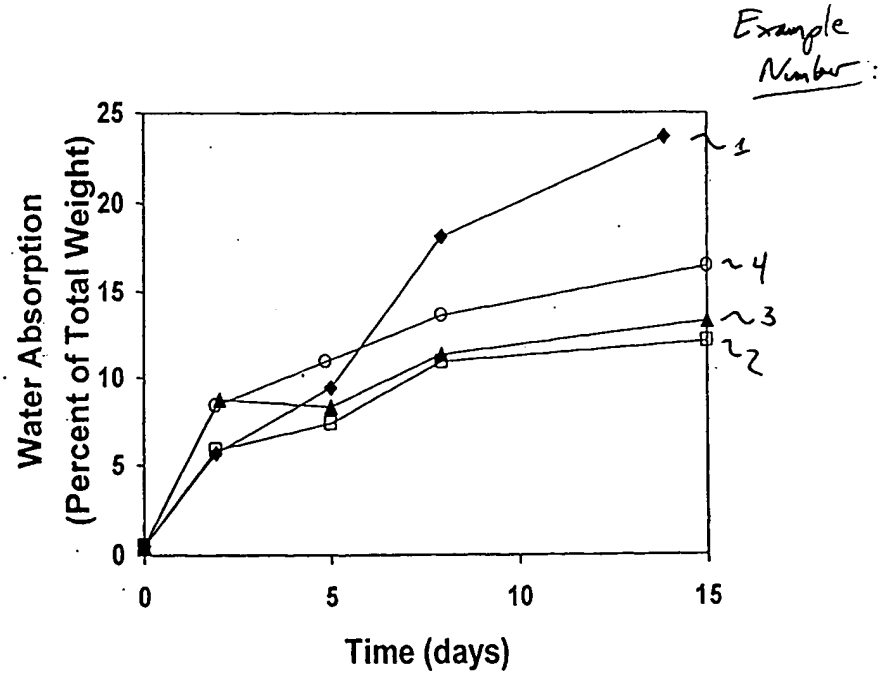

Figure 5 is a graph comparing protein release from the exemplary compositions. The rate of release of the protein is dependent on the relative amounts of crystallizable and amorphous polymer in these compositions. Figure 10 is a graph comparing the water absorbed by the exemplary compositions. The behavior of these compositions in an aqueous environment is also dependent on the relative amounts of crystallizable and amorphous polymer in the formulation.

The rejection of the claims over Tipton et al., Ruiz, or Brodbeck et al., alone or in combination, has been obviated by appropriate amendment. Claim 1 has been amended to include a biodegradable amorphous polymer.

Tipton et al. describes a biodegradable film dressing which can be used to protect and/or deliver a bioactive agent to an area of tissue (col. 2, lines 5-12). The Examples (1-10) describe biodegradable compositions containing a single copolymer of D,L-lactide and ε-caprolactone. This is a single polymer, not a mixture. Tipton et al. lists a wide variety of biodegradable polymers and "mixtures therein" (col. 5, lines 8-19). There is no description that the polymers in the list are either crystallizable or amorphous. For reasons relating to solubility, Tipton et al. prefers polymers having a low ability to crystallize, and does not suggest combinations of crystallizable and amorphous polymers (col. 5, lines 32-34).

Ruiz describes a drug delivery formulation containing a biodegradable polymer in a biodegradable oil vehicle (col. 1, lines 20-27). The Examples (1, 3, 6, 9 and 11) describe biodegradable compositions containing a single copolymer of D,L-lactide and glycolic acid. This is a single polymer, not a mixture. There is no mention of combinations of biodegradable polymers.

Brodbeck et al. describes an implantable gel for drug delivery. The Examples (1, 2 and 8) describe biodegradable compositions containing a single copolymer of D,L-lactide and glycolic acid (see also Tables 1 and 2). This is a single polymer, not a mixture. Brodbeck et al. lists a wide variety of biodegradable polymers and "mixtures thereof" (col. 10, line 65 through col. 11, line 7). There is no description that the polymers in the list are either crystallizable or amorphous.

The claims now include a biodegradable crystallizable polymer and a biodegradable amorphous polymer. Tipton et al., Ruiz, and Brodbeck et al. do not describe the use of a combination of a biodegradable crystallizable polymer and a biodegradable amorphous polymer. Copolymers prepared from different monomers are not a combination of different polymers. Rather, a single copolymer is prepared from a mixture of monomers. Although lists of polymers are provided, there is no suggestion to select an amorphous polymer together with a crystallizable polymer.

Further evidence of unobviousness is provided by comparison of Examples 1-5 from the present application. These examples, and the associated Figures 5 and 10 reproduced above, illustrate the unexpected and surprising results obtained by the use of a combination of a biodegradable crystallizable polymer and a biodegradable amorphous polymer. Both the release of the bioactive agent and the water absorption characteristics can be varied by controlling the relative amounts of crystallizable polymer and amorphous polymer in the compositions. For example, the presence of a crystallizable polymer may provide for a rapid release of the bioactive agent. The type and relative amount of crystallizable polymer may affect both the timing and the amplitude of the rapid release. There is nothing in the applied references to suggest these results. These unexpected and surprising results demonstrate the unobviousness of the claimed invention.

Applicants submit that the claimed invention is neither anticipated by, nor obvious over, the applied references. Widthdrawal of these rejections is respectfully requested.

The rejection of the claims under 35 USC §112 is respectfully traversed. The preamble of Claim 21 states that the claimed composition is for the controlled release of a bioactive agent; however Claim 21 does not require the presence of the bioactive agent. The bioactive agent and the composition can then be combined to provide a composition containing the bioactive agent (page 15, line 25 through page 16, line 13). Claims 27 and 41 are thus not indefinite, as they merely recite the composition containing the beneficial agent.

Also filed at this time is a Supplemental Information Disclosure Statement, with FORM PTO-1449 and cited references.

Applicants submit that the application is in condition for allowance. Early notice of such action is respectfully requested.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (Amended) A composition for controlled release of a bioactive agent, comprising:

a biodegradable crystallizable polymer;

a biodegradable amorphous polymer;

a biocompatible solvent; and

a bioactive agent.

17. (Amended) The composition of claim 1[9], wherein the biodegradable amorphous polymer is a polyester.

18. (Amended) The composition of claim 1[9], wherein the biodegradable amorphous polymer is poly(D,L-lactide).

36. (Amended) A method of administering a bioactive agent, comprising: inserting the composition of claim 27[21] into an organism.

38. (Amended) A method of making the composition of claim 1, comprising: combining ingredients;

wherein said ingredients comprise a biodegradable crystallizable polymer; a biodegradable amorphous polymer; a biocompatible solvent; and a bioactive agent.